One Health and cancer: A comparative study of human and canine cancers in Nairobi

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Abstract

Aim: Recent trends in comparative animal and human research inform us that collaborative research plays a key role in deciphering and solving cancer challenges. Globally, cancer is a devastating diagnosis with an increasing burden in both humans and dogs and ranks as the number three killer among humans in Kenya. This study aimed to provide comparative information on cancers affecting humans and dogs in Nairobi, Kenya.

Materials and Methods: Dog data collection was by cancer case finding from five veterinary clinics and two diagnostic laboratories, whereas the human dataset was from the Nairobi Cancer Registry covering the period 2002-2012. The analysis was achieved using IBM SPSS Statistics® v.20 (Dog data) and CanReg5 (human data). The human population was estimated from the Kenya National Census, whereas the dog population was estimated from the human using a human:dog ratio of 4.1:1.

Results: A total of 15,558 human and 367 dog cancer cases were identified. In humans, females had higher cancer cases 8993 (an age-standardized rate of 179.3 per 100,000) compared to 6565 in males (122.1 per 100,000). This order was reversed in dogs where males had higher cases 198 (14.9 per 100,000) compared to 169 (17.5 per 100,000) in females. The incident cancer cases increased over the 11-year study period in both species. Common cancers affecting both humans and dogs were: Prostate (30.4, 0.8), the respiratory tract (8.3, 1.3), lymphoma (5.6, 1.4), and liver and biliary tract (6.3, 0.5), whereas, in females, they were: Breast (44.5, 3.6), lip, oral cavity, and pharynx (8.8, 0.6), liver and biliary tract (6.5, 1.2), and lymphoma (6.0, 0.6), respectively, per 100,000.

Conclusion: The commonality of some of the cancers in both humans and dogs fortifies that it may be possible to use dogs as models and sentinels in studying human cancers in Kenya and Africa. We further infer that developing joint animal-human cancer registries and integrated cancer surveillance systems may lead to accelerated detection of the risks of cancer in Africa.

Keywords: Africa, cancer, cancer registry, comparative oncology, Kenya, Nairobi, One Health.

Introduction

One Health and cancer

The study of cancer through comparative oncology, in recent times, has provided invaluable insights on how the pet-dog is not only man's companion but also plays an integral role in improving human health and well-being [1,2]. More importantly, reiterating the added value of One Health [3] by acting or having the potential to act as sentinels (early warning systems) and models for studying, early diagnosis and treatment of human cancer and possibly other animals as well.

Cancer registries

Cancer registries play an important role of facilitating early detection, prevention, treatment, and care of cancer patients. In Kenya, there are two human population-based cancer registries: Geographical positioned in Nairobi and Eldoret counties, three hospital-based registries, and three other registries are in their early stages of development. On 10th February 2016, the Kenya National Cancer Registry Programme was launched [4]. However, there is no animal cancer registry in the country.

The burden of cancer

Worldwide, cancer continues to torment man [5] and dog [6-8] alike, with the global burden increasing in both species. Cancer is among the four noncommunicable diseases (NCDs) responsible for 82% deaths attributable to NCDs, with three quarters of these occurring in low- and middle-income countries [9].

In Kenya, cancer ranks as the number three cause of mortality among humans, after infectious diseases and cardiovascular diseases, with the number of cancer cases projected to nearly double by 2030 [10]. This has and will continue to escalate the "double burden" of disease, with an accompanying dual effect of not only straining existing health-care systems [5,10]

but also causing loss of income to already poor families and posing cumulative economic losses. The challenge of addressing cancer in Kenya has been attributed to several technical, economic, infrastructural, and social factors [11]. The burden of cancer among animals, in this case pet-dogs, is unknown in this study setting; but, there is a general observation from the practicing clinicians that cancer cases among pet-dogs are on the rise.

Are dogs' better models and sentinels for human cancers?

The dog is of special interest compared to other laboratory [12] and domestic animals in studying human cancer because: It naturally and increasingly develops spontaneous cancer similar to humans [7], which could be as a result of the increasing "human-dog bond" which increases their exposure to similar risk factors and environmental carcinogens [13]. Moreover, the dog is phylogenetically closely related to man [14]; this is supported by the fact that approximately all the 19,000 genes identified in the dog match to a similar gene in the human genome [15].

Several studies have documented that pet-dogs respond to a number of environmental carcinogens, similar to the way humans do [16-20]. For instance, the association between industrial activity and consequent bladder cancer has been established [17], with the dog having a shorter latent period of bladder cancer (10 years), as compared to man (20 years) [14]. Thus, humans and dogs do develop similar cancers when exposed to similar risk factors or carcinogens, and by inference, monitoring the health of pet-dogs (and potentially other animals as well) will aid early identification and correlation between exposure to environmental contaminants and cancer in humans [21].

The aim of the study

In Kenya, the comparative aspect of studying cancers in humans and animals at the same time has not been explored. There also lacks a system for collecting population data on animal cancers similar to the human cancer registries. The objective of the study was, therefore, to determine the most common cancers affecting humans and dogs by age and gender in Nairobi area so as to determine the potential of using dogs as models and sentinels for human cancers. We presume the results to catalyze future research ventures for comparison with other populations within and elsewhere and to complement the current national and global efforts geared toward cancer prevention and control.

Materials and Methods

Ethical clearance and approval

Approval and an introductory letter seeking permission to access data from the human cancer registry, veterinary clinics, and laboratories was issued by the Faculty of Veterinary Medicine, University of Nairobi dated 24th January 2013. For the human data, being secondary data, the corresponding scientific and ethical approvals are described [22, 23].

Study area

Nairobi County is the primary capital city of Kenya with a population of 3,138,369 (1,605,230 males and 1,533,139 females) based on the 2009 census [24]. It has a fairly good representation of the population and ethnic groups in Kenya. Pet animal population and structure are not available for Nairobi County, but it is home to a large number of veterinary practices and with the highest population of dogs kept as pet-dogs.

Human data methodology

The human data methodologies detailing on data collection, data variables, sources of information, data management, computer applications, coding, and classification have been described in an earlier report of 2006 by the Kenya Medical Research Institute [22] and a recent publication by Korir *et al*. [23]. The following sections will dwell on the dog methodologies.

Tumor data sources

Dog datasets were actively extracted from seven institutions within Nairobi County, of which five were veterinary clinics and two were reference veterinary diagnostic laboratories. The dataset comprised five sets of diagnostic records from necropsy/postmortem, laboratory (cytology and histology), clinical investigation (radiography), medical records, and index cards mentioning cancer as the contributory cause of morbidity or mortality, spanning from the year 2002 to 2012. However, only one veterinary clinic had a computer-based disease index system. In all cases, the clinic and laboratory personnel were involved to provide the required information.

Data variables

Dog data were keyed into a preconfigured Microsoft Access 2013® database with the number of assessment variables used based on the standards provided by the International Agency for Research on Cancer as outlined by MacLennan [25] but with modifications to fit the veterinary case records and for comparison with the human records. The variables included were: The patient details (Unique ID, breed, sex, and age), the tumor details (date of diagnosis, entered as year only), the basis of diagnosis, topography (first occurrence only), morphology (based on histology/cytology), the source of information (entered as name of clinic), mode of treatment, and patient status (entered as alive or dead, as at date of data extraction).

Data preparation

Dog datasets were exported from the Microsoft Access 2013® database into IBM SPSS v20. Before exporting each data, variable was coded separately (Table-1).

Data collection

Human and dog data collection was by desk review through scheduled visits to veterinary clinics, laboratories, and the human cancer registry between

Table-1: Dog dataset as coded in IBM SPSS v. 20.

Variable name	Type	Measure	Label	Values
Unique ID	Numeric	Scale	Unique patient identifier	Incremental by 1 from 1000
Breed	String	Nominal	Breed of dog	Based on the 22 breeds of dogs identified (coded 00-21, 99)
Sex	Numeric	Scale	Sex of dog	0=Male, 1=Female
Age	Numeric	Scale	Age of dog	Value entered as recorded
Status	Numeric	Nominal	Status of dog on data abstraction	0=Dead, 1=Alive, 9=Unknown
Incidence	Date	Scale	Date of first registration of case	Value entered as recorded
Topography	String	Nominal	3-digit code of the tumor site	Values coded based on the online ICD-0-3 [57] and data available
Morphology	Numeric	Nominal	4-digit code of the tumor morphology	Values coded based on the online ICD-0-3 [57] and data available
Behavior	Numeric	Nominal	Behavior of tumor	0=Benign, 1=Uncertain, 2=*In situ*, 3=Malignant
Diagnosis	Numeric	Nominal	Basis of diagnosis of tumor	0=Necropsy, 1=Clinical only, 2=Clinical investigation, 3=Surgery/Autopsy, 4=Laboratory tests, 5=Cytology, 6=Histology primary
Treatment	Numeric	Nominal	Mode of treatment	0=Medical only, 1=Surgery, 2=None, 3=Unknown, 4=Euthanasia
Facility	Numeric	Nominal	The source name of data	Each facility coded individually 0-6

August 2013 and April 2014. The dog data were entered directly into the preconfigured Microsoft Access 2013® database, whereas the human data were retrieved and downloaded from the Canreg5 database as a tab-separated values file format.

Population data

Human annual intercensal estimates were projected using annual growth rates for the 5-year age group and for each gender based on 1999 [26] and 2009 [24] census data for Nairobi County (Table-2). Since the Nairobi County dog population and structure is not known, the corresponding total dog population at each 5-year age group was calculated using the ratio of humans to dogs as 4.1:1 [27]. The corresponding dog numbers for each gender were calculated using the dog male:female ratio of 1.4:1 [27]. Based on the 11-year (2002-2012) population estimates, the calculated Nairobi County annual average human population was 2,991,704 (1,506,182 males and 1,406,159 females) and the dogs as 729,605 (425,603 males, 304,002 females) are shown in Figure-1 for the human and dog population pyramids.

Data analysis

Results are presented as the number of cancer cases registered, crude, and age-standardized incidence rates, for the study period (2002-2012). The crude, all ages rate per 100,000 was calculated by dividing the total number of cases per site by the total number of person/dog-years of observation and multiplying the result by 100,000. The age-specific rate for each age group was calculated as a rate per 100,000 by dividing the number of cases in the age group by the corresponding person/dog-years of observation and multiplying the result by 100,000.

Age-standardized rates (ASRs) per 100,000 were calculated by the direct method using the World Standard Population (for human) and using a known

and published age structure for the dog [28] as an external standard but with modifications to fit study age groupings (Table-3). The cancer cases of unknown age were further included in the determination of ASR by multiplying with a correction factor. 95% confidence intervals for the ASR were also calculated. All calculations described above were done as per guidelines by Boyle and Parkin [29].

Results

Dog and human datasets

During the 11-year period (2002-2012) under review, a total of 15,558 human cancer cases (age-standardized incidence rate of 137.4 per 100,000) were retrieved from the human cancer CanReg5 database, consisting of 6565 (42.2%) male (ASR of 122.1 per 100,000) and 8993 (57.8%) female cancer cases (ASR of 179.3 per 100,000). In dogs, 367 cancer cases (ASR of 16.0 per 100,000) were retrieved, of which 198 (54.0%) were males (ASR of 14.9 per 100,000) and 169 (46.0%) female cancer cases (ASR of 17.5 per 100,000) shown in Table-4 for a detailed record of the ASRs for each topographical site and species and their corresponding 95% confidence intervals.

Trend of cancer cases

The number of cancer cases increased progressively over the study period in both humans and dogs as shown in Figure-2. Whereas this was generally true, the spontaneous decrease in the number of incident cases was observed in the years 2007 and 2009 in both humans and dogs.

Incidence of the top 10 cancers by topography affecting both humans and dogs

The common cancers affecting both male humans and dogs (among the top 10 cancers) were: Prostate (ASR of 30.4, 0.8 per 100,000), respiratory tract (ASR of 8.3, 1.3 per 100,000), lymphoma (ASR of 5.6, 1.4 per 100,000), and liver and biliary tract (ASR of 6.3,

0.5 per 100,000), respectively. The common cancers affecting both female humans and dogs (among the top 10 cancers) were: Breast (ASR of 44.5, 3.6 per 100,000), lip, oral cavity, and pharynx (ASR of 8.8, 0.6 per 100,000), liver and biliary tract (ASR of 6.5,

1.2 per 100,000), and lymphoma (ASR of 6.0, 0.6 per 100,000), respectively (Figure-3).

Cancer cases and age-specific incidence per age group in humans and dogs

The number of cancer cases and age-specific rates per 100,000 in both humans and dogs generally increased with advancing age. The highest number of cancer cases affected humans of 40-44 age-group (but the highest age-specific rate was at 70-74 age group), whereas, in dogs, the highest cancer cases affected the 11-12 age-group (but the highest age-specific rate was at 15+ age group). By gender, most cancer cases in female humans and dogs were recorded in (40-44; 11-12) and (75+; 11-12) age groups, respectively, whereas, in male, humans and dogs they were recorded in (75+; 15+) age-groups, respectively (Table-5).

Breed and cancer distribution

The dataset included 23 different dog breeds (Supplementary Material-1). Of the 23.7% cross-breeds, 6.9% were between a German Shepherd Dog (GSD) and another known breed, 10.3% were crosses of other known breeds, and 82.8% were crosses of other unknown/unrecorded breeds, simply indicated as "cross" in the records. It was evident that

Table-2: Annual growth rates for the 5-year age group and for each gender.

Age group	Annual growth rates	
	Male (%)	Females (%)
0-4	4.1	4.0
5-9	4.8	4.7
10-14	4.1	3.4
15-19	2.3	2.1
20-24	2.1	4.4
25-29	2.9	5.2
30-34	3.7	5.8
35-39	4.0	5.6
40-44	3.9	5.7
45-49	4.2	6.2
50-54	2.8	5.3
55-59	5.4	7.0
60-64	5.3	6.2
65-69	4.2	5.4
70-74	2.9	3.4
75+	2.5	4.7

Table-3: Deriving the dog standard population using a known standard population published by Thrusfield [28].

Age interval (years)[a]	Male[b]	Female[c]	Total[d]	% Male[e]	% Female[f]	% Total[g]	Male[h]	Female[i]	Total[j]	Age class[k]	Dog standard population[l]
<1	378,000	365,000	743,000	12	12	11.6	11,732	11,521	11,628	0-2 mo	2907
<1-≤2	433,000	365,000	798,000	13	12	12.5	13,439	11,521	12,488	3-5 mo	2907
<2-≤3	378,000	365,000	743,000	12	12	11.6	11,732	11,521	11,628	6-8 mo	2907
<3-≤4	287,000	320,000	607,000	9	10	9.5	8908	10,101	9499	9-11 mo	2907
<4-≤5	287,000	279,000	566,000	9	9	8.9	8908	8807	8858	1-2	12,488
<5-≤6	239,000	238,000	477,000	7	8	7.5	7418	7513	7465	3	11,628
<6-≤8	416,000	447,000	863,000	13	14	13.5	12,911	14,110	13,505	4	9499
<8-≤10	323,000	323,000	646,000	10	10	10.1	10,025	10,196	10,110	5	8858
<10-≤12	220,000	244,000	464,000	7	8	7.3	6828	7702	7261	6-7	7465
<12-≤14	174,000	152,000	326,000	5	5	5.1	5400	4798	5102	8	13,505
>14	87,000	70,000	157,000	3	2	2.5	2700	2210	2457	9	5055
	3,222,000	3,168,000	6,390,000	100	100	100.0	100,000	100,000	100,000	10	5055
										11-12	7261
										13	5102
										14	1228
										15+	1228
										Total	100,000

[a]Age intervals as described by Thrusfield [28], [b]Number of males per age intervals as described by Thrusfield [28], [c]Number of females per age intervals as described by Thrusfield [28], [d]Total number of dogs per age intervals as described by Thrusfield [28], [e]Calculated % = Number of males in class interval divided by total number of males multiplied by 100, [f]Calculated % = Number of females in class interval divided by total number of females multiplied by 100, [g]Calculated % = Total number of dogs in class interval divided by summed total number of dogs multiplied by 100, [h]Weighted number for male dogs = Value in column (b) multiplied value in column (e) for each class, [i]Weighted number for male dogs = Value in column (c) multiplied value in column (i) for each class, [j]Weighted number for male dogs = Value in column (d) multiplied value in column (g) for each class, [k]The 16 age groupings as per the current study to be comparable to the human 16 age groupings, [l]Equally distributed from the values in column (j) and in reference to the age intervals in column (a)
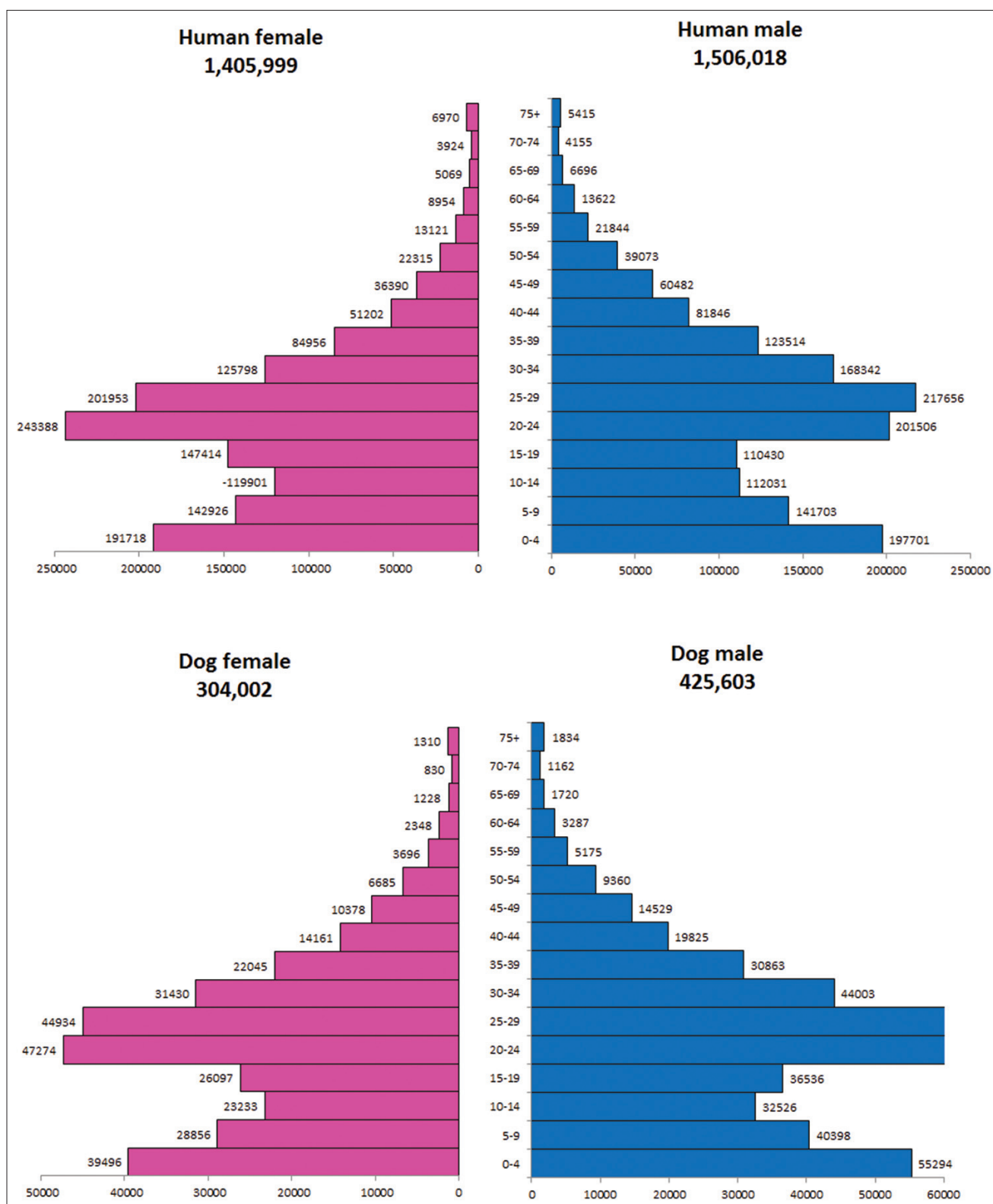
Figure-1: Composition by sex and 5-year age group of the average population for humans and dogs in Nairobi, (2002-2012).

common cancers affecting the top breeds in Nairobi were breast and skin cancers, of which they affected at a higher proportion, the German shepherd breed (breast - 3.0%), and the crossbreeds (skin - 2.2%).

The distribution of the most common morphological diagnoses and staging

The common individual morphological diagnoses in humans and dogs were neoplasm,

malignant-8000 (14.3%, 44.4%), squamous cell carcinoma, NOS-8070 (19.5%, 6.5%), adenocarcinoma, NOS-8140 (13.8%, 4.6%), and malignant lymphoma, NOS-9591 (1.3%, 8.4%), respectively (Figure-4).

The staging distribution of human cancers was as follows: Unknown stage (88.7%), Stage III (2.5%), Stage IV (2.3%), Stage II (2.1%), and Stage I (0.9%), excluding the invalid codes (3.6%), whereas,

Table-4: ASRs (at 95% CI) for humans and dogs by gender and topography/site in Nairobi, 2002–2012.

Name	ICD (10th)	Male humans			Female humans			Male dogs			Female dogs		
		No. cases (%)	Crude	ASR (95% CI)	No. cases (%)	Crude	ASR (95% CI)	No. cases (%)	Crude	ASR (95% CI)	No. cases (%)	Crude	ASR (95% CI)
Lip, oral cavity and pharynx	C00-14	742 (11.3)	4.8	11.6 (6.7-16.6)	416 (4.6)	2.7	8.8 (7.9-9.7)	3 (1.5)	0.1	0.0	6 (3.6)	0.2	0.6 (0.4-0.9)
Esophagus	C15	592 (9.0)	3.8	12.2 (6.3-18.2)	415 (4.6)	2.7	11.5 (10.3-12.6)	1 (0.5)	0.0	0.1 (−0.2-0.4)	1 (0.6)	0.0	0.0
Stomach	C16	406 (6.2)	2.6	8.2 (3.5-12.9)	305 (3.4)	2.0	8.0 (7.1-8.9)	0 (0.0)	0.0	0.0	0 (0.0)	0.0	0.0
Small intestine	C17	12 (0.2)	0.1	0.3 (0.4-0.9)	6 (0.1)	0.0	0.1 (0.0-0.1)	0 (0.0)	0.0	0.0	0 (0.0)	0.0	0.0
Colon	C18	303 (4.6)	2.0	5.6 (1.9-9.3)	253 (2.8)	1.6	5.9 (5.2-6.7)	0 (0.0)	0.0	0.0	0 (0.0)	0.0	0.0
Rectum	C19-20	207 (3.2)	1.3	4.0 (0.6-7.5)	163 (1.8)	1.1	3.4 (2.8-3.9)	1 (0.5)	0.0	0.0	0 (0.0)	0.0	0.0
Anus	C21	11 (0.2)	0.1	0.2 (0.6-1.0)	19 (0.2)	0.1	0.5 (0.3-0.7)	9 (4.5)	0.2	1.7 (1.2-2.2)	4 (2.4)	0.1	0.3 (−0.1-0.7)
Liver and biliary tract	C22-24	351 (5.3)	2.3	6.3 (2.2-10.4)	273 (3.0)	1.8	6.5 (5.7-7.3)	12 (6.1)	0.3	0.5 (0.4-0.7)	12 (7.1)	0.4	1.2 (0.5-2.0)
Pancreas	C25	126 (1.9)	0.8	3.0 (0.1-5.9)	110 (1.2)	0.7	2.9 (2.3-3.4)	1 (0.5)	0.0	0.0	1 (0.6)	0.0	0.0
Intestinal tract, part unspecified	C26.0	0 (0.0)	0.0	0.0	0 (0.0)	0.0	0.0	2 (1.0)	0.0	0.0 (0.0-0.1)	1 (0.6)	0.0	0.6 (0.1-1.0)
Spleen	C26.1	0 (0.0)	0.0	0.0 (0.0-0.0)	0 (0.0)	0.0	0.0	12 (6.1)	0.3	0.7 (0.5-0.9)	9 (5.3)	0.3	0.4 (0.0-08)
Respiratory tract	C30-34	366 (5.6)	2.4	8.3 (3.5-13.1)	162 (1.8)	1.0	3.8 (3.2-4.4)	13 (6.6)	0.3	1.3 (1.0-1.6)	9 (5.3)	0.3	0.9 (0.3-1.5)
Others and unspecified thoracic organs	C37-38	7 (0.1)	0.0	0.1 (0.4-0.6)	17 (0.2)	0.1	0.4 (0.2-0.6)	3 (1.5)	0.1	0.1 (0.0-0.2)	0 (0.0)	0.0	0.0
Bone	C40-41	193 (2.9)	1.2	2.1 (0.3-3.9)	154 (1.7)	1.0	2.2 (1.7-2.6)	9 (4.5)	0.2	1.1 (0.7-1.6)	10 (5.9)	0.3	1.5 (0.9-2.2)
Skin	C43-44	138 (2.1)	0.9	2.5 (0.1-5.1)	145 (1.6)	0.9	3.3 (2.8-3.9)	37 (18.7)	0.8	3.5 (2.8-4.2)	36 (21.3)	1.1	4.7 (3.4-6.0)
Mesothelioma	C45	2 (0.0)	0.0	0.1 (0.3-0.4)	1 (0.0)	0.0	0.0 (0.0-0.1)	0 (0.0)	0.0	0.0	0 (0.0)	0.0	0.0
Kaposi sarcoma	C46	319 (4.9)	2.1	2.6 (0.9-4.4)	163 (1.8)	1.1	1.4 (1.101.6)	0 (0.0)	0.0	0.0	0 (0.0)	0.0	0.0
Connective and soft tissue	C47, 49	113 (1.7)	0.7	1.0 (0.0-2.1)	106 (1.2)	0.7	1.5 (1.1-1.8)	19 (9.6)	0.4	0.3 (0.2-0.3)	9 (5.3)	0.3	0.1 (0.0-0.1)
Breast	C50	97 (1.5)	0.6	1.9 (0.3-4.1)	2278 (25.3)	14.7	44.5 (42.7-46.4)	0 (0.0)	0.0	0.0	40 (23.7)	1.2	3.6 (2.9-4.3)
Vulva and vagina	C51-52	0 (0.0)	0.0	0.0 (0.0-0.0)	70 (0.8)	0.5	1.4 (1.1-1.8)	0 (0.0)	0.0	0.0	13 (7.7)	0.4	0.6 (0.3-0.9)
Cervix uteri	C53	0 (0.0)	0.0	0.0 (0.0-0.0)	1890 (21.0)	12.2	35.8 (34.1-37.5)	0 (0.0)	0.0	0.0	0 (0.0)	0.0	0.0
Others and unspecified part of uterus	C54-55	0 (0.0)	0.0	0.0 (0.0-0.0)	273 (3.0)	1.8	7.3 (6.508.2)	0 (0.0)	0.0	0.0	1 (0.6)	0.0	0.2 (0.0-0.3)
Ovary	C56	0 (0.0)	0.0	0.0 (0.0-0.0)	298 (3.3)	1.9	6.5 (5.7-7.2)	0 (0.0)	0.0	0.0	0 (0.0)	0.0	0.0
Others and unspecified parts of female organs	C57-58	0 (0.0)	0.0	0.0 (0.0-0.0)	15 (0.2)	0.1	0.1 (0.0-0.2)	0 (0.0)	0.0	0.0	0 (0.0)	0.0	0.0

(*Contd....*)

Table-4: *Continued...*

Name	ICD (10th)	Male humans			Female humans			Male dogs			Female dogs		
		No. cases (%)	Crude	ASR (95% CI)	No. cases (%)	Crude	ASR (95% CI)	No. cases (%)	Crude	ASR (95% CI)	No. cases (%)	Crude	ASR (95% CI)
Penis	C60	19 (0.3)	0.1	0.3 (0.5-1.1)	0 (0.0)	0.0	0.0	17 (8.6)	0.4	1.0 (0.5-1.4)	0 (0.0)	0.0	0.0
Prostate	C61	1006 (15.3)	6.5	30.4 (19.9-41.0)	0 (0.0)	0.0	0.0	19 (9.6)	0.4	0.8 (0.3-1.3)	0 (0.0)	0.0	0.0
Testis	C62	21 (0.3)	0.1	0.3 (−0.7-1.2)	0 (0.0)	0.0	0.0	7 (3.5)	0.1	0.5 (0.3-0.6)	0 (0.0)	0.0	0.0
Others and unspecified parts of male organs	C63	6 (0.1)	0.0	0.1 (−0.5-0.7)	0 (0.0)	0.0	0.0	2 (1.0)	0.0	0.4 (0.0-0.9)	0 (0.0)	0.0	0.0
Kidney, etc.	C64-66	69 (1.1)	0.4	1.1 (−0.6-2.8)	92 (1.0)	0.6	1.2 (0.9-1.4)	0 (0.0)	0.0	0.0	1 (0.6)	0.0	0.6 (0.1-1.0)
Bladder	C67	113 (1.7)	0.7	2.9 (−0.2-6.0)	52 (0.6)	0.3	1.3 (1.0-1.7)	2 (1.0)	0.0	0.4 (0.3-0.6)	1 (0.6)	0.0	0.1 (0.0-0.2)
Others and unspecified parts of urinary system	C65-66, 68	0 (0.0)	0.0	0.0 (0.0-0.0)	2 (0.0)	0.0	0.1 (0.0-0.1)	0 (0.0)	0.0	0.0	1 (0.6)	0.0	0.4 (0.2-0.6)
Eye	C69	254 (3.9)	1.6	2.6 (0.6-4.6)	285 (3.2)	1.8	3.0 (2.6-3.4)	6 (3.0)	0.1	0.4 (0.1-0.7)	3 (1.8)	0.1	0.3 (0.4-1.1)
Brain, nervous system	C70-72	155 (2.4)	1.0	2.1 (0.2-4.0)	147 (1.6)	1.0	2.1 (1.7-2.6)	3 (1.5)	0.1	0.1 (0.1-0.2)	1 (0.6)	0.0	0.0
Endocrine system	C73-75	37 (0.6)	0.2	0.5 (−0.7-1.8)	135 (1.5)	0.9	2.6 (2.1-3.0)	0 (0.0)	0.0	0.0	0 (0.0)	0.0	0.0
Lymphoma	C81-88, C90	461 (7.0)	3.0	5.6 (2.6-8.7)	355 (3.9)	2.3	6.0 (5.3-6.7)	10 (5.1)	0.2	1.4 (1.0-1.9)	2 (1.2)	0.1	0.6 (0.2-1.0)
Leukemia	C90-95	181 (2.8)	1.2	1.9 (0.1-3.8)	146 (1.6)	0.9	2.1 (1.7-2.5)	0 (0.0)	0.0	0.0	0 (0.0)	0.0	0.0
Other and unspecified	O&U	258 (3.9)	1.7	4.1 (0.7-7.5)	247 (2.7)	1.6	5.3 (4.6-6.0)	10 (5.1)	0.2	0.4 (0.2-1.1)	8 (4.7)	0.2	0.8 (0.5-1.0)
All sites		6565 (100.0)	42.4	122.1 (103.8-140.4)	8993 (100.0)	58.1	179.3 (175.4-183.2)	198 (100.0)	4.2	14.9 (13.3-16.6)	169 (100.0)	5.1	17.5 (15.2-19.8)

ICD-O-[10th]=International Classification of Diseases for Oncology, 10th edition, No. cases=Total number of incident cases per site/topography, Crude=Crude rate per 100,000, ASR=Age-standardized rate per 100,000, 95% CI=95% confidence interval given in brackets
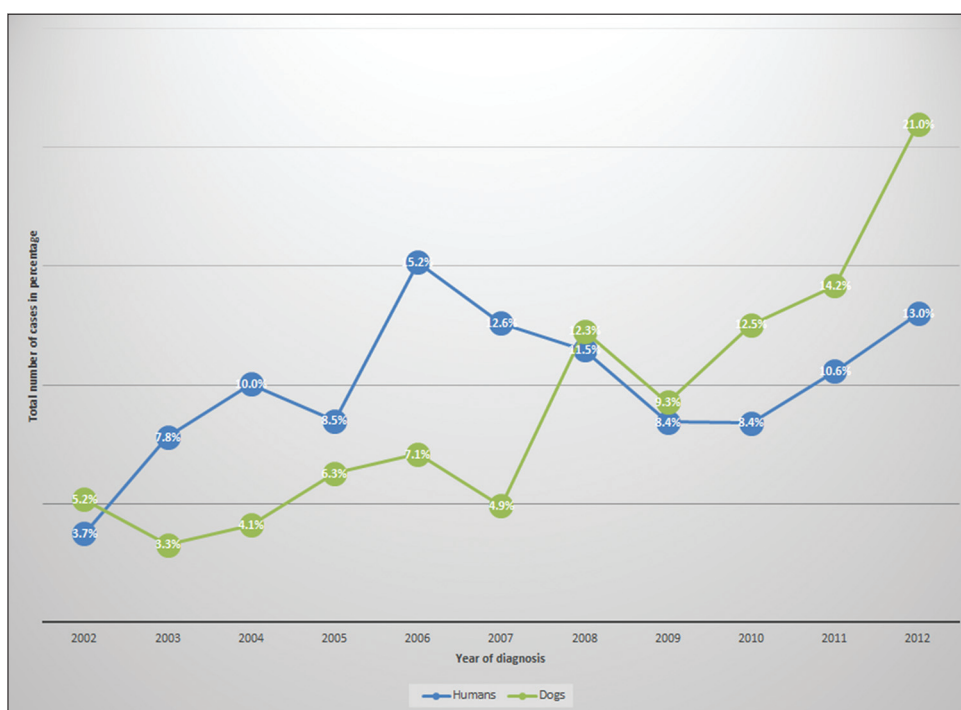
Figure-2: Trend of incident cancer cases in human and dogs in Nairobi (2002-2012).

Table-5: Number of cancer cases and age-specific rates per age group in humans and dogs.

Human years	Dog years*	Human (n=15,542)***			Dog (n=181)***			Event**
		Male	**Female**	**Total**	**Male**	**Female**	**Total**	
0-4	0-2 months	129 (5.9)	115 (5.5)	244 (5.7)	0 (0.0)	0 (0.0)	0 (0.0)	
5-9	3-5 months	135 (8.7)	73 (4.6)	208 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	
10-14	6-9 months	139 (11.3)	99 (7.5)	238 (9.5)	0 (0.0)	0 (0.0)	0 (0.0)	Puberty range in most women and bitches
15-19	10-11 months	166 (13.7)	135 (8.3)	301 (10.7)	0 (0.0)	0 (0.0)	0 (0.0)	
20-24	1-2	204 (9.2)	238 (8.9)	442 (8.6)	3 (0.4)	6 (1.2)	9 (0.7)	
25-29	3-4	241 (10.1)	422 (19.0)	663 (13.6)	3 (0.4)	1 (0.2)	4 (0.3)	
30-34	4-5	347 (18.7)	685 (49.5)	1032 (30.3)	6 (1.2)	4 (1.2)	10 (1.2)	
35-39	5-6	410 (30.2)	924 (98.9)	1334 (55.9)	5 (1.5)	5 (2.1)	10 (1.7)	
40-44	6-7	560 (62.2)	1124 (199.6)	1684 (109.9)	12 (5.5)	5 (3.2)	17 (4.5)	The start of increased cancer of all types in both species
45-49	8-9	587 (88.2)	1082 (270.3)	1669 (148.6)	8 (5.0)	5 (4.4)	13 (4.7)	
50-54	9-10	613 (142.6)	981 (399.6)	1594 (220.3)	4 (3.9)	8 (10.9)	12 (6.8)	
55-59	10-11	546 (227.2)	851 (589.6)	1397 (349.2)	16 (28.1)	12 (29.5)	28 (28.7)	
60-64	11-12	662 (441.8)	742 (753.3)	1404 (552.4)	23 (63.6)	15 (58.1)	38 (61.3)	
65-69	13-14	571 (775.2)	542 (972.1)	1113 (837.2)	5 (26.4)	7 (51.8)	12 (37.0)	
70-74	14-15	547 (1196.8)	448 (1038.0)	995 (1107.7)	4 (31.3)	2 (21.9)	6 (27.4)	
75+	15+	702 (1178.6)	522 (680.8)	1224 (863.1)	8 (39.6)	14 (97.1)	22 (63.6)	A reasonable equivalent of an upper age extreme for both species

*Age conversion using Lebeau [58] and the online access tool Available from: http://www.pedigree.com/all-things-dog/dog-age-calculator/. **Events common to both species as described by Lebeau [58]. ***Only cases of known age are included (values in brackets are the age-specific rates per 100,000)

in dogs, no staging was done on any of the morphological diagnoses. The proportional distribution of diagnostic methods for the dog cancers were necropsy/post-mortem (41.7%), followed by clinical only (25.3%), histology primary (14.7%), laboratory tests (9.0%), surgery/autopsy (8.4%), cytology (0.5%), and clinical investigation (0.3%). The data quality indicators for the human records from the Nairobi Cancer Registry showed that 98.5% of the records were valid for analysis (excluding those with unknown age), 83.6% were confirmed through laboratory analysis, 15.6% diagnosed through clinical
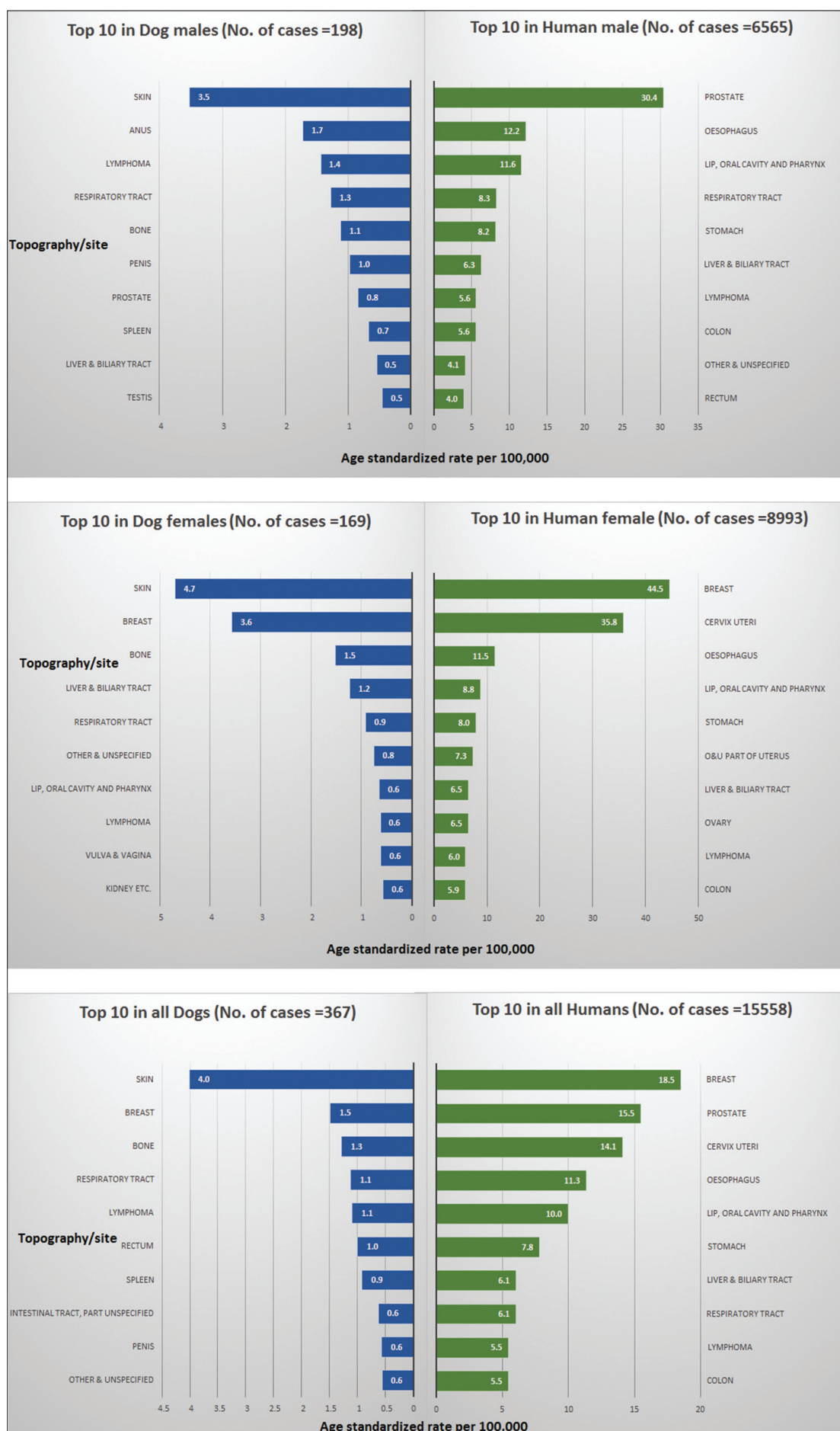
Figure-3: Top 10 most common cancers in male and female humans and dogs in Nairobi (2002-2012).
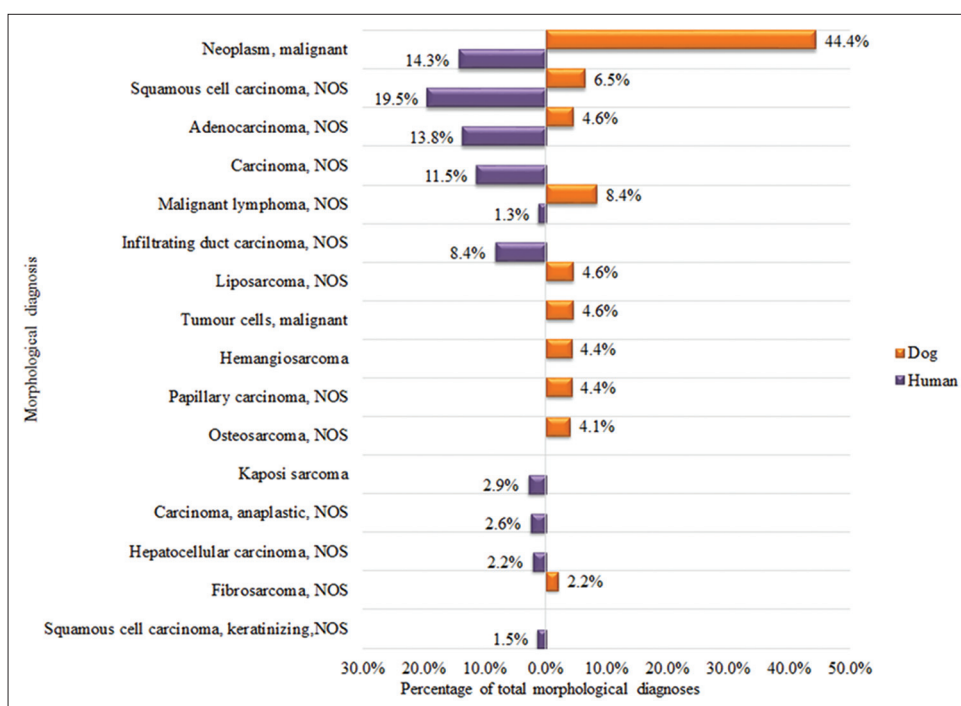
Figure-4: Common morphological diagnoses of cancer in humans and dogs in Nairobi (2002-2012).

investigation, and only 0.8% were diagnosed through the certificate of death.

Discussion

Dataset and methods

The difference between the number of cancer cases retrieved for the human dataset (n=15,558) compared to dogs (n=367) could be explained by a wider institutional coverage of the human dataset (27 facilities) [22] as compared to the canine data (7 facilities). However, the dog and human data do provide a comparative basis of certain cancer sites since they take into account the size and characteristics of the population at risk. Further, the human and dog data collection did not only rely on pathology departments but also traced clinically diagnosed cases.

Due to lack of dog population numbers for Nairobi County, estimates were calculated using the published human:dog ratio of 4.1:1 [27]. This ratio 4.1:1 was preferred since it represents an urban population setting that is comparable to the study population, i.e., Kisumu and Nairobi are both urban cities in Kenya. The lack of pet animal demographic data is a common phenomenon across the entire country. There is, therefore, need for the government of Kenya to integrate small animals (dogs and cats) into the National Census, which will also support other intervention strategies such as rabies control that require knowledge of the dog population. We further suggest that developing a World Standard Population for dogs could complement future comparative oncology studies, especially when it comes to comparing ASRs; this is based on the fact that most studies that are published and which we have referenced [13,30-32] (excluding Dobson *et al.* [33]) that investigated cancer in dogs

and cats reported the percentage of cases rather than ASRs. This, therefore, makes it difficult to compare accurately the cancer incidence between different populations [29].

Trend of cancer

The increasing number of cancer cases, with advancing in age, in both humans and dogs in Nairobi is consistent with reports on the occurrence of various cancers from other parts of the world [34] and as also reported by other studies in California-Davis [13], Italy-Genoa [31], and in the UK [33]. The increasing number of cancer cases could be attributed to: An actual increase in cancer cases in both humans and dogs; an increase in the population at risk of developing cancers; an increasing proportion of facilities offering veterinary and human medical [35] services, or an increased awareness level and interest to undertake diagnostic and therapeutic options for cancer [1]. Further, this increase can be as a result of the changes taking place in Kenya such as socioeconomic development, accessibility to regional and international markets, demographic changes, and rapid urbanization and modernization [35]. These factors result to an accelerated exposure to cancer risk factors such as lifestyle change, access to unhealthy foods (high fat and high salt) and consumer products for both human and dog populations.

It was not possible to explain why there was a depressed number of cases in the year 2007 while, for the year 2009, it could be attributable to the postelection chaos that could have resulted in a low attendance to health facilities.

Cancer incidence by gender

The number of cancer cases in humans and dogs was almost equally distributed in both genders, which

contrast findings by Merlo et al. [31], who found a 3-fold higher incidence in females than male dogs. The slightly higher cancer cases in human females could be attributed to the higher mammary and cervical cancers, at the same time the publicity for cancer screening among females in Nairobi may have contributed to the higher frequency in the number of cases, rather than the occurrence of cancer. Another plausible reason could be that females have a higher tendency of health-seeking behavior as compared to males. The occurrence of a higher age-standardized cancer rate among female dogs although their population and cancer cases were lower as compared to male dogs, could infer that female dogs could be having a higher predisposition to cancer or the frequency of cancer occurrence in females is higher as compared to males. Future studies are needed to explain the causal mechanisms for this phenomenon.

Age and cancer

The number of cancer cases in both humans and dogs was clearly associated with age and also as observed by Dobson et al. [33] in the UK, Merlo et al. [31] in Italy, and the 2014 World Cancer Report [34]. In humans, cancer cases peaked at the 40-44 age group in women and at 75+ age group in men, which was a similar finding from the World Cancer Report [34] in sub-Saharan Africa. In female dogs, cancer cases peaked at the 11-12 age group and the +15 age group in males, similar to findings by Dobson et al., 2002 (>9 years) [33], Merlo et al., 2008 (>9-11 years) [31], and slightly with Grüntzig et al., 2015 (between 5 and 10 years) [32].

It is significant to note that cancer peaks later in both human and dog males as compared to the females, this can possibly be explained by the earlier age onset of breast and cervical cancers in females and later age onset of prostate cancers in males [34]. It is also evident that dogs are frequently affected by cancers between the age of >9 years similar to findings by Dorn et al. [13], which is much earlier than in man [14]. This may potentially facilitate the detection of hazards and risk factors for cancer earlier in dogs than in humans.

Breed predisposition to cancer

The overrepresentation of the GSD breed and crossbreed is similar to findings by Grüntzig et al., 2015 [32]; this finding could be because they are common utility breeds and commonly used for security purposes in most developing nations, Kenya inclusive. The distribution of most of the cancers by both topography and morphology was more related to the number of cases reported than the dog breed, and therefore, the effect of breed on the cancer cases in this study was generally not clear, but the GSD was differentially predisposed to the hemangiosarcoma while the Labrador to the mast cell tumor, but this could not conclusively be established as compared to the study by Dobson et al. [36].

The most common cancers by topography in both humans and in dogs

Despite the short period of study (2002-2012), the data collected so far does show consistency and specific contrasts with reports on the occurrence of various cancers from other parts of the world [34], Africa (Supplementary Material-2), and other dog and comparative research studies (Supplementary Material-3).

In this study, we have observed that there are common cancers that affect both humans and dogs and some disproportionately affecting a certain gender. This does infer a possibility of common environmental carcinogens or risk factors. For example, liver cancers (probably as a result of aflatoxins [37], hepatitis B and C infection [38,39] or indiscriminate alcohol consumption [22,40]; respiratory cancers (probably due to chronic smoking in humans [41], passive smoking and other environmental exposures, e.g. diesel exhaust, arsenic in water, etc., for both), lymphoma (as a result of viral carcinogen [42], lifestyle charges and chemicals), and age/hormonal/lifestyle change/urbanization [43] in case of prostate [44] and breast/mammary gland cancers [45-47]. This does show a potential for future studies (in Kenya or Africa) to use dogs as models to study prostate, breast/mammary gland, and lymphoma cancers and as sentinels for liver and respiratory cancers. Several studies have already shown this possibility of using dogs as sentinels [16-20] and models [7,15] for studying human cancers.

Tumor diagnostic approaches

At the tumor level, the most common individual morphological tumor diagnosis in humans and dogs were approximately as one would expect based on estimates from previous studies in dogs [48] and humans [34]. A commonality in both humans and dogs in regard to morphological diagnosis and staging in this study was the high number of ICD-O code 8000, and the unknown staging (88.7%) in humans and with no staging in dogs. In dogs, this could possibly be explained by findings on diagnostic approaches, where the detection and diagnosis of tumors vary according to objective difficulties and methodologic difference among veterinary clinics as also noted by Brønden et al. [7]. Contrary, in humans, most of the diagnoses are confirmed through laboratory techniques, which is commendable. Irrespective of this, it is crucial to remember that very few people in developing countries (including Kenya) can manage the cost of cancer diagnosis (not mentioning treatment), and therefore, this informs us that there are still many cancer cases that are not captured or reported in this study. Future studies should focus on bridging this gap to identify the unreported cases through community-based cancer studies, so as to determine the true burden of cancer.

In this study, most tumors in dogs were diagnosed at postmortem (41.7% of all cases) and clinical only (25.3% of all cases), with laboratory methods contributing (32.9% of all cases). The fact that most

cases were diagnosed as deceased shows that there is a high mortality rate of canine patients diagnosed with cancer although the causes of death may not be as a result of these cancers. Cancer diagnosis involving a combination of careful clinical assessment and diagnostic investigations is the first step to cancer management, but in a developing country like Kenya most of the cancer diagnostic methods are rare or limited and also the cost involved is high, partly explaining the diagnostic outcome.

Conclusion and Recommendations

An 11-year comparative study is relatively a short period for comments on general trends for disease, including cancer. However, despite the short period, data collected so far does show a consistency and specific contrasts with reports on the occurrence of various cancers from other parts of the world, region, and other comparative research studies in both humans and dogs. We would also like to highlight that cancer registration is a difficult enterprise in Africa, faced by a number of shortcomings making the distribution of most cancer registries in Africa confined to the urban populations, Mali [49], Guinea [38], Zimbabwe [50], Ivory coast [51], Uganda [52], Malawi [53], except the Gambia [54] that has a cancer registry with a national coverage [54].

Perhaps the most important contribution that this study makes is providing for the first time from a developing nation, Kenya, comparative aspects of cancers in dogs and humans in the same geographical area. From the results, it is clear that more comparative research adopting integrative and SMART One Health approaches are required. Since many dogs in Kenya and many parts of Africa share with humans common environments and lifestyle and since cancer in both has a clinical and histological similarity, the potential for using dogs as models and sentinels is present. At the same time, dog breeding over time has resulted in clear breed-predisposition to certain cancer types. This implies both an excellent model for genetic risk factors in cancer development and also possibility to investigate protective genotypes as well which, in fact, could explain higher and lesser predisposition to respond to a certain environmental carcinogen.

As we have noted in this study, dogs are frequently affected by cancers at a much earlier time than man similar to findings by Dorn *et al.* [13]; this may potentially facilitate detection of risks and hazards earlier in dogs than humans. Future sentinel studies should, therefore, be planned to assess this possibility. This can only be achieved with well-established "comparative" cancer registries that provide accurate data to allow spatial identification of differences in low and high human and/or dog risk populations and thus providing clues into the etiology of cancer. More importantly, there is need to strengthen the existing human cancer registries since as of now

cancer is one of the primary objectives for African governments [55]. There is need for the veterinary surgeons and pathologists in Kenya to start thinking of developing a cancer surveillance system which may be integrated to the human cancer registry. We also recommend and encourage that all cancer diagnoses, especially staging of cancer in dogs, to be reported using internationally standardized formats, which will provide a strong basis for future comparative research. However, there are still challenges that have to be overcome, such as the stigma driven by traditional beliefs which prevent people from seeking screening and diagnosis and limited resources, especially the crucial resource of knowledge.

In conclusion, we reiterate that Africa can win the battle against cancer through collaborative public health action through the One Health movement [56], and through innovations and training in comparative oncology research through complementary intra-Africa and North-South collaborations.

Authors' Contributions

NKM conducted the research and actively prepared the manuscript. NKM and REM designed the work. REM and RAK participated in the manuscript preparation and advice during the research work. All the authors read and approved the final manuscript.

Acknowledgments

Competing Interests

The authors declare that they have no competing interests.

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Supplementary Materials
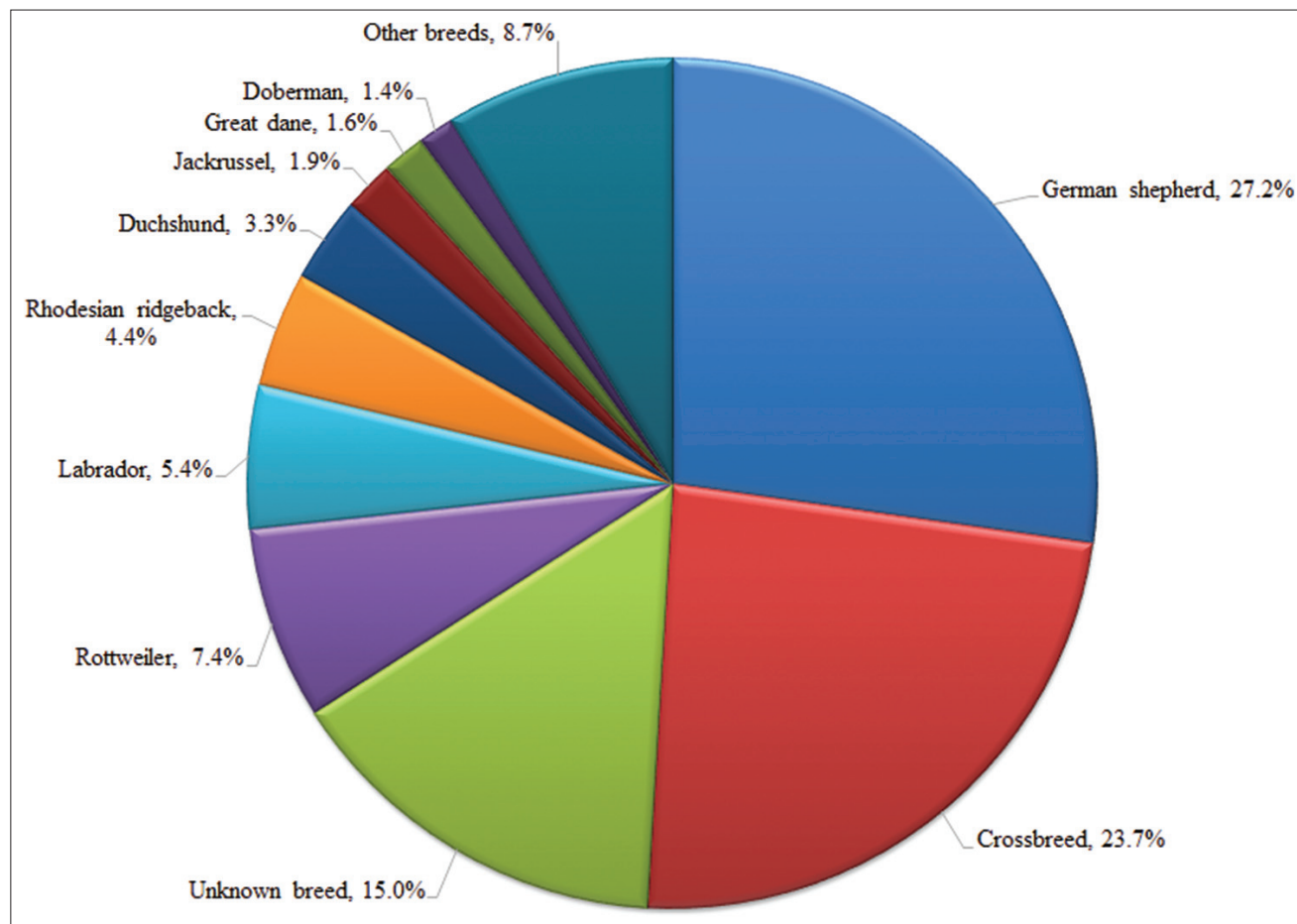
Supplementary Material 1: Dog breed distribution in Nairobi (2002-2012).

Supplementary Material-2: Top five most common cancers in 10 human registries in Africa in terms of their incidence.

Rank	CR*1 [1]	CR*2 [1]	CR*3 [1]	CR* [1]	CR*5 [1]	CR*6 [2]	CR*7 [3]
1	M: Liver F: Cervix	M: Lung F: Cervix	M: Liver F: Cervix	M: Liver F: Liver	M: Liver F: Cervix	M: Liver F: Cervix	M: Liver F: Cervix
2	M: NHL F: Breast	M: Liver F: Liver	M: Prostate F: Breast	M: Stomach F: Cervix	M: Stomach F: Liver	M: Prostate F: Liver	M: Esophagus F: Breast
3	M: Prostate F: NHL	M: Prostate F: Breast	M: Stomach F: Liver	M: NHL F: Breast	M: Bladder F: Stomach	M: Stomach F: Breast	M: Prostate F: Liver
4	M: Stomach F: Stomach	M: Bladder F: Stomach	M: Bladder F: Bladder and colorectum	M: Prostate F: Stomach	M: Lung F: Breast	M: Lung F: Stomach	M: Kaposi's sarcoma F: Stomach
5	M: Leukemia F: Liver AND leukemia	M: Stomach F: Bladder	M: Colorectum F: NHL	M: Lung F: NHL	M: Prostate F: Bladder	M: Bladder F: Ovary	M: Lung F: Bladder

Rank	CR*8 [3]	CR*9 [4]	CR*10 [5]	CR*11 [6]	CR*12 [7]	CR*13 [8]	CR*14 [9]
1	M: Kaposi's sarcoma F: Cervix	M: Prostate F: Cervix	M: Kaposi's sarcoma F: Cervix	M: Liver F: Cervix	M: Kaposi's sarcoma F: Cervix	M: Prostate F: Breast	M: Prostate F: Breast
2	M: Liver F: Breast	M: Liver F: Breast	M: Prostate F: Breast and Kaposi's sarcoma	M: Lung F: Liver	M: Esophagus F: Kaposi's sarcoma	M: Esophagus F: Cervix	M: Mouth F: Cervix uteri
3	M: Prostate F: Kaposi's sarcoma	M: Lung F: Liver	M: Esophagus F: Colorectum	M: Prostate F: Breast	M: Prostate F: Breast	M: Colorectal F: Esophagus	M: Esophagus F: Esophagus
4	M: Esophagus F: Liver	M: Stomach F: Stomach	M: Stomach F: Liver	M: NHL F: Corpus Uteri	M: Liver F: NHL	M: Stomach F: Colorectal	M: Stomach F: Mouth
5	M: Lung F: Stomach	M: NHL F: Ovary	M: NHL F: NHL	M: Stomach F: Stomach	M: Bladder and NHL F: Thyroid	M: Oral cavity F: Stomach	M: Respiratory F: Stomach

CR*1=Ibadan, Nigeria 1960-69, CR*2=Bulawayo, Zimbabwe 1968-72, CR*3=Dakar, Senegal, 1969-74, CR*4=Gambia 1986-88, CR*5=Bamako, Mali 1987-88, CR*6=Guinea, Conakry 1992-95, CR*7=Harare, Zimbabwe 1990-92, CR*8=Harare, Zimbabwe 1993-95, CR*9=Abidjan, Ivory Coast 1995-1997, CR*10=Kampala, Uganda 1995-1997, CR*11=Gambia, 1988-97, CR*12=Blantyre, Malawi 1994-1998, CR*13=Nairobi, Kenya, 2004-2008. CR=Cancer registry, NHL=Non-Hodgkin lymphoma, M=Male, F=Female

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Supplementary Material-3: The top five most common cancers in six dog cancer registries in terms of percent of total cases.

Rank	CR*1 [1]	CR*2 [2]	CR*3 [3]	CR*4 [4]	CR*5 [5]	CR*6
1	M: Skin F: Mammary gland	M: Skin F: Mammary gland	Skin and soft tissue	M: NHL F: Mammary gland	Skin	M: Skin F: Skin
2	M: Connective tissue F: Skin	M: Testis F: Oral cavity	Alimentary	M: Skin F: NHL	Mammary gland	M: Anus F: Breast
3	M: Testis F: Connective tissue	M: Oral cavity F: Vagina/vulva	Mammary	M: Male genital organs F: Connective and soft tissue	Soft tissue	M: Lymphoma F: Bone
4	M: Mouth and pharynx F: Lymphosarcoma	M: Eye F: Ovary	Urogenital	M: Connective and soft tissue F: Skin	Gastrointestinal	M: Respiratory tract F: Liver and biliary tract
5	M: Lymphosarcoma F: Mouth and pharynx	M: Spleen F: Eye	Lymphoid	M: Lip, oral cavity, and pharynx F: Digestive organs and peritoneum	Male sexual organs	M: Bone F: Respiratory tract

CR*1=Alamada and Contra Costa, California 1963-1966, CR*2=Norwegian Canine Cancer Project, 1990-1998, CR*3=UK, 1997-1998, CR*4=Genoa, Italy, 1985-2002, CR*5: Switzerland, 1955-2008, CR*6: Nairobi, 2002-2012. CR=Cancer registry, NHL=Non-Hodgkin lymphoma, M=Male, F=Female

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